

### **REMARKS/ARGUMENTS**

Claim 16 has been revised to more explicitly indicate the nature of the featured “9-cis retinal derivative” as not being “9-cis retinal”. Instead, and as expressly indicated in the claim, the featured “derivative” is defined as being a “9-cis retinal” with “a modification of the polyene chain but with retention of the polyene chain length and retention of the 9-cis bond”.

Dependent Claims 19 and 20 have been canceled without prejudice for re-presentation in a continuing application.

No new matter has been introduced, and entry of the revised claims is respectfully requested.

#### **Information Disclosure Statement (IDS)**

The Action mailed November 15, 2009 indicates that the IDS filed September 23, 2009 was not accompanied by a copy of each of the 13 cited documents.

Applicants have reviewed the Image File Wrapper (IFW) for the instant application at the Office’s website using “public PAIR” and point out that the IFW shows 13 “NPL” documents entered on September 23, 2009 with the submitted IDS.

Applicants respectfully submit that no further copies of the documents are necessary and that they should be considered and formally made of record in the instant application.

#### **Claim Objections**

The Action mailed November 15, 2009 indicates that Claims 19 and 35 did not include the proper claim identifiers. Applicants thank the Office for noting the minor clerical errors in those claim identifiers.

Applicants have carefully reviewed the claim identifiers in the above revised claims to ensure that they are correct.

Applicants believe no substitute copy of the claims filed July 27, 2009 *with correct identifiers* is being required. However, Applicants are prepared to submit a substitute copy if so required.

Reconsideration of the objections is respectfully requested.

*Election/Restriction Requirement*

Applicants thank the Office for indicating that there is no current election of species requirement for the pending claims. So there is no current requirement for election of a specific compound or between oral and local administration.

Accordingly, Applicants withdraw their previous voluntary shift in elected species from 11-cis-7-ring retinal (elected via the response filed February 8, 2008) to the compound encompassed by Claim 20. Furthermore, Claim 20 has been canceled as indicated above.

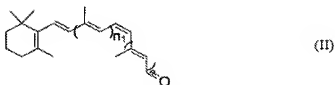
*Alleged Rejection Under 35 U.S.C. § 112, first paragraph*

Claims 16-20, 35-37, and 49-51 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants have carefully reviewed the statement of this rejection and respectfully traverse because no *prima facie* case of “new matter” is present.

The statement of the rejection alleges that paragraphs [0031] and [0037] of US 2004/0242704 (the U.S. Pat. Publication of the instant application) fails to adequately support the “9-cis retinal derivative” featured in the claims. Applicants respectfully disagree and first point out that as an initial matter, the term “9-cis retinal derivative” clearly indicates that the compound is a derivative of “9-cis retinal”. Additionally, a “9-cis retinal derivative” is clearly a “synthetic retinoid” as disclosed in the instant application.

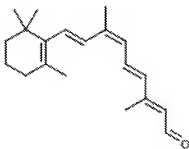
Second, support for the term “9-*cis* retinal derivative” is found in part in paragraph [0030] and Formula II on page 8 of the instant application (identical to paragraph [0031] in US 2004/0242704) as reproduced below:

[0030] The synthetic retinoid also can be a derivative of an 11-*cis*-retinal or 9-*cis*-retinal that has a modified polyene chain length of the following formula II:



The polyene chain length can be extended by 1, 2, or 3 alkyl, alkene or alkylene groups. According to formula II, each  $n$  and  $n_1$  can be independently selected from 1, 2, or 3 alkyl, alkene or alkylene groups, with the proviso that the sum of the  $n$  and  $n_1$  is at least 1.

Clearly, Formula II and paragraph [0030] describe a “synthetic retinoid” that is “a derivative” of the following 9-*cis* retinal structure based upon Formula II, where  $n$  and  $n_1$  are each 1:



Moreover, paragraph [0030] discloses that this 9-*cis* retinal structure may optionally have a “modified polyene chain length”. This is disclosure of the alternative possibilities of a polyene chain with and without a change in the chain length, and so either one may be excluded via the language of the claims. See *In re Johnson* 558 F.2d 1008, 1019, 194

USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). So paragraph [0030] and Formula II clearly support the features of "retention of the polyene chain length and retention of the 9-*cis* bond" in Claim 16.

Applicants next direct the Office's attention to the first sentence in paragraph [0033], bridging pages 9 and 10 of the instant application, as reproduced below:

[0033] The synthetic retinoid can further be a derivative of an 11-*cis*-retinal or 9-*cis*-retinal that has a modified polyene chain. Suitable derivatives include, for example, those with a *trans/cis* locked configuration, 6s-locked analogs, as well as modified allene, alkene, alkyne or alkylene groups in the polyene chain. In one example, the derivative is an 11-*cis*-locked analog of the following formula VII:

Applicants respectfully point out that contrary to the statement of the instant rejection, the first sentence of paragraph [0033] is not clearly not limited to disclosed Formula VII. Instead, the first sentence is generally applicable to each "synthetic retinoid" of the instant disclosure. This must include a derivative of the 9-*cis* retinal structure shown above based upon paragraph [0030] and Formula II. Therefore, paragraph [0033] clearly supports the feature of "a modification of the polyene chain" as present in Claim 16.

In light of the above, no *prima facie* case of "new matter" or an inadequate written description is present, and this rejection may be properly withdrawn.

*Alleged Rejections Under 35 U.S.C. § 112, second paragraph*

Claims 16-20, 35-37, and 49-51 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicants have carefully reviewed the statement of this rejection and respectfully traverse for the following reasons.

First, and with respect to the instant rejection as alleged based on Claims 19 and 20, Applicants respectfully point out that those two claims have been canceled. Accordingly, the rejection based thereon may be properly withdrawn.

Next, and with respect to the instant rejection based upon the term “derivative,” Applicants respectfully point out that the express language of Claim 16 provides sufficient clarity regarding claim scope to a skilled person in the art. More specifically, the term “derivative” is not used in isolation. Instead, Claim 16 clearly states that the “derivative” is a structurally based on 9-cis retinal with the following explicit features:

- the derivative “is not 9-cis retinal” and so must be structurally different from 9-cis retinal;
- the derivative “is a modification of the polyene chain” (emphasis added) present in 9-cis retinal;
- the derivative has “retention of the polyene chain length” present in 9-cis retinal; and
- the derivative has “retention of the 9-cis bond” that is present in 9-cis retinal.

As indicated by the above, the derivatives featured in Claim 16 cannot “be anything” as alleged in the statement of the rejection. Instead, only derivatives of 9-cis retinal that meet the above listed features are encompassed.

The instant rejection also alleges that it is “unclear what constitutes a modification of the polyene chain, whether it is substitution off the chain or substitution of elements of the chain.” In response, Applicants point out that both substitutions off the chain and substitution of elements in the chain are clearly encompassed in a broad, but not indefinite manner. The Office’s attention is directed to MPEP 2173.04 and the case decisions cited therein, setting forth the standard that breadth is not indefiniteness.

The legal standard that breadth is not indefiniteness also applies to the alleged questions regarding “the aldehyde of the retinal” because the hydrogen atom of the aldehyde is attached to a carbon atom in the polyene chain. Therefore, the skilled person would clearly understand that the hydrogen atom, as well as the oxygen atom attached to the same carbon atom, is an element of the chain subject to substitution as encompassed by the phrase “modification of the polyene chain”.

In light of the foregoing, Applicants respectfully submit that no case of indefiniteness is present and that this rejection may be properly withdrawn.

*Alleged Rejections Under 35 U.S.C. § 103*

Claims 16-19, 35-37 and 49-51 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Chapple et al. (ANCR, 3(1):12-13, 2003). Applicants have carefully reviewed the statement of the rejection as well as the cited document and respectfully traverse because no *prima facie* case of obviousness is present.

Before addressing the statement of rejection and the cited document, Applicants point out that the Office has failed to provide adequate evidence that Chapple et al. is cited as art under 35 U.S.C. § 102(b). The guidance set forth at MPEP 2128.02 and in the case decisions cited therein indicate the need for an affidavit to establish factors such as normal time frame and practice for publication and delivery for access by the public. But the copy of the email from publisher Rachael Hansford fails to demonstrate a date of public availability of Chapple et al. The statement by Ms. Hansford does not indicate first-hand knowledge of the publication process in the time period of March and April, 2003. It isn't even clear that Ms. Hansford was the Publisher at that time. Additionally, satisfaction of the requirements of 35 U.S.C. § 102(b) cannot be based upon Ms. Hansford's guess. Accordingly, Applicants understand Chapple et al. as cited under 35 U.S.C. § 102(a) until adequate evidence to the contrary is provided.

Chapple et al. report that "addition of 9-cis retinal to cultures expressing P23H mutant opsin improves the amount of opsin that reaches the plasma membrane whilst having no effect on K296E mutant opsin" (see page 13, left column, last paragraph, first sentence).

Applicants have explained above how the claims do not encompass administration of 9-cis retinal. Moreover, Chapple et al. fail to teach or suggest a 9-cis retinal derivative as featured in the claims. Therefore, the skilled person would receive no guidance and no expectation of success from Chapple et al. to arrive at the claimed invention.

Accordingly, this rejection may be properly withdrawn.

Claims 35-37 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Chapple et al. (as cited above) in view of Lang (Adv. Drug Deliv. Rev. 16(1):39-43, 1995) and Geroski et al. (IOVS 41(5):961-964, 2000). Applicants have carefully reviewed the statement of the rejection as well as the cited documents and respectfully traverse because no *prima facie* case of obviousness is present.

The deficiency of Chapple et al. has been explained above. The documents by Lang and Geroski et al., whether each is taken alone or in combination with the other, fail to teach or suggest a 9-cis retinal derivative as featured in the claims. Accordingly, no combination of the cited documents can lead a skilled person to the claimed invention. Therefore, this rejection may be properly withdrawn.

Conclusion

In light of the foregoing, Applicants respectfully submit that the claims are allowable and urge early indication to that effect. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at number below.

Respectfully submitted,

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